

Incidence and Procedural Risk Factors for Symptomatic Cholecystitis After Yttrium-90 Transarterial Radioembolization: A Systematic Review and Meta-analysis

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Abstract

Purpose

To estimate the incidence of clinically symptomatic cholecystitis after yttrium-90 transarterial radioembolization (Y-90 TARE) and synthesize evidence on procedural risk factors.

Methods

A multibase literature search was screened against prespecified criteria. Adult Y-90 cohorts reporting an exact symptomatic-event numerator and patient denominator were eligible. Imaging-only abnormalities were excluded. Incidence was pooled with a random-intercept binomial-normal generalized linear mixed model; zero-event cohorts were retained.

Results

Forty-four reports met the eligibility criteria. Excluding one likely overlapping cohort left 43 independent cohorts, 5,380 patients, and 67 events. Pooled incidence was 1.32% (95% profile-likelihood confidence interval, 0.88%–1.89%); the approximate 95% prediction interval was 0.28%–6.05%. Leave-one-out estimates ranged from 1.24% to 1.46%. Comparative evidence did not support routine permanent cystic-artery coiling. Gallbladder imaging abnormalities were poorly specific for clinical disease.

Conclusion

Clinically symptomatic cholecystitis after Y-90 TARE is uncommon but varies across settings. Careful mapping and distal catheter positioning when tumor coverage permits are supported; routine permanent cystic-artery embolization is not. Take-home message: Symptomatic cholecystitis occurs in approximately 1.3% of patients, and prevention should prioritize anatomy-guided catheter positioning rather than routine permanent cystic-artery coiling.

Introduction

Yttrium-90 transarterial radioembolization (Y-90 TARE), also termed selective internal radiation therapy, delivers beta-emitting microspheres through hepatic arterial branches to treat primary and metastatic liver malignancies. The treatment is generally well tolerated, but nontarget delivery can injure extrahepatic structures. The gallbladder is vulnerable because the cystic artery most often arises from the right hepatic arterial circulation and may lie near a planned treatment position.

Post-treatment cholecystitis may reflect radiation, ischemia, or both. Microspheres reaching the cystic arterial bed can irradiate the gallbladder wall, whereas coil or particulate occlusion, vasospasm, or flow redistribution can produce ischemic injury. Published reports describe radiogenic, embolic, ischemic, acalculous, and unspecified cholecystitis, and they use different time windows and severity thresholds [1–4].

The procedural literature also presents a difficult prevention question. Operators may position the treatment catheter distal to the cystic-artery origin, alter the treatment territory, or embolize the cystic artery with temporary or permanent material. Other reports describe intentional treatment through a cystic-artery tumor supply. These strategies are selected according to anatomy and indication, so comparisons are vulnerable to confounding by indication [2, 5–8].

This review estimates the incidence of clinically symptomatic cholecystitis after Y-90 TARE and examines procedural factors associated with risk. It separates clinical disease from imaging-only gallbladder abnormalities and retains zero-event cohorts in a rare-proportion meta-analysis.

Materials and Methods

Review Question and Eligibility Criteria

The review asked: among adults undergoing Y-90 TARE for primary or metastatic hepatic malignancy, what is the incidence of clinically symptomatic cholecystitis, and which procedural or technical factors are associated with its occurrence?

Eligible reports described human adult cohorts treated with Y-90 glass or resin microspheres and provided an exact patient-level numerator and denominator for symptomatic post-treatment cholecystitis. Prospective and retrospective cohorts, registries, trials, and technique-focused series with more than 10 participants were eligible. Reports were excluded when they described another intervention, lacked a valid patient denominator, reported only imaging abnormalities, were reviews or isolated case reports, or represented an overlapping cohort that could not be separated. An explicit zero-event statement was eligible; silence about cholecystitis was treated as missing outcome information.

Information Sources and Search

The sensitive literature containing records from PubMed/MEDLINE, CINAHL, and Google Scholar yielded 796 records. The export covered database inception through September 22, 2026. Search concepts combined terms for yttrium-90, radioembolization or selective internal radiation therapy, gallbladder or cystic artery, cholecystitis, nontarget embolization, and adverse events. Citation chaining identified additional reports. Search and reporting methods followed PRISMA 2020 and PRISMA-S principles [9, 10].

Study Selection and Data Extraction

Records underwent title and abstract screening followed by detailed eligibility assessment. Extracted fields included study design, population, sample size, microsphere type, treatment territory, cystic-artery anatomy and management, mapping method, gallbladder uptake, clinical outcome definition, follow-up, symptomatic events, timing, management, mortality, and procedural factors. Reports describing the same or likely overlapping cohort were linked, and only one contributed to the primary independent-cohort model.

Study selection and data extraction were performed by multiple reviewers with a predetermined process to resolve any discrepancies. Risk-of-bias judgments were also independently reviewed. Disagreements were resolved through discussion and consensus, with adjudication by a third reviewer if required. The review was prospectively registered on PROSPERO [11, 12].

Outcomes

The primary outcome was the cumulative incidence proportion of clinically symptomatic cholecystitis after Y-90 TARE, calculated as unique patients with a new clinical diagnosis divided by unique treated patients. Imaging-only gallbladder uptake, wall thickening, enhancement, or pericholecystic change without compatible clinical disease did not meet the primary outcome. Secondary outcomes included timing, suspected mechanism, hospitalization, antibiotics, conservative management, cholecystostomy, cholecystectomy, cholecystitis-related mortality, and procedural associations.

Risk of Bias

Study-level appraisal used JBI-informed concepts for incidence and cohort evidence [13]. Domains addressed participant selection, denominator validity, outcome definition, adequacy of follow-up, cohort independence, and applicability. Judgements were low risk, some concerns, or high risk.

Statistical Analysis

For each cohort, exact binomial 95% confidence intervals were calculated. The primary pooled estimate used a one-stage random-intercept binomial-normal generalized linear mixed model with a logit link and seven-point adaptive Gauss-Hermite quadrature. Zero-event studies were retained without continuity correction. The pooled result represents the median underlying incidence across settings, with a profile-likelihood confidence interval for the intercept [14].

Between-study heterogeneity was summarized with tau and tau-squared on the logit scale and an auxiliary I-squared estimate from a maximum-likelihood logit-proportion model. The approximate prediction interval was calculated as the inverse-logit transformation of the fitted mean plus or minus 1.96 tau; it describes dispersion of underlying risks but does not propagate all model-parameter uncertainty. Sensitivity analyses restricted the model to general or mapping cohorts, anatomy- or technique-enriched cohorts, explicit all-grade symptomatic ascertainment, etiologically compatible cohorts, and studies published from 2015 onward. Leave-one-out analyses evaluated influence.

Procedural factors were synthesized narratively because comparisons were sparse, nonrandomized, and clinically nonexchangeable. The funnel plot was exploratory. It did not serve as a heterogeneity measure or formal publication-bias test because rare proportions and their standard errors are mathematically linked, and conventional asymmetry tests can be misleading.

Results

Study Selection

The consolidated database export contained 796 records, and citation chaining added 16 records. Of 812 unique records screened, 685 were excluded during title and abstract screening. Detailed assessment was performed for 127 candidate reports; 83 were excluded after full-text or detailed abstract assessment. Forty-four reports met the eligibility criteria. One report was judged likely to overlap with a larger cohort, leaving 43 independent cohorts for meta-analysis.

Figure 1 Study identification, screening, eligibility, and quantitative inclusion. The consolidated export was representing PubMed/MEDLINE, CINAHL, and Google Scholar. One likely overlapping report was excluded from the independent-cohort model.

Characteristics of Included Reports

Table 1

Characteristics of the 44 included reports. *Atassi et al. [1] was retained in the qualitative review but excluded from the independent-cohort model because of likely cohort overlap. CA, cystic artery; HCC, hepatocellular carcinoma.

Study	Design	Population	Microspheres	Events/patients	Cohort type	Meta-analysis
Carr 2004 [15]	Prospective single-center safety cohort	HCC	Glass (TheraSphere)	2/65	General cohort	Yes
Jiao 2007 [16]	Prospective observational cohort	Unresectable primary/metastatic liver tumors	Resin	1/21	General cohort	Yes
Atassi 2008 [1]*	Retrospective imaging/toxicity cohort	HCC (190) and liver metastases (137)	Mixed/NR	2/327	General cohort	No*
Kennedy 2009 [17]	Retrospective multicenter registry	Primary and metastatic hepatic tumors	Resin	0/515	General cohort	Yes
Cianni 2010 [18]	Observational single-center cohort	Unresectable hepatic metastases	Resin	2/110	General cohort	Yes
McWilliams 2011 [2]	Retrospective technical cohort	Hepatic malignancies requiring right-lobar TARE	Not reported	3/46	Anatomy/management enriched	Yes
Lenoir 2012 [19]	Prospective/retrospective imaging-planning cohort	Primary and metastatic hepatic tumors	Not reported	2/89	General mapping cohort	Yes
Peterson 2013 [20]	Two-center consecutive cohort	Unresectable hepatic tumors	Mixed/NR	7/112	General cohort	Yes
Theysohn 2013 [5]	Retrospective consecutive cohort	Primary and metastatic hepatic tumors	Not reported	1/295	General mapping cohort	Yes
Bester 2014 [21]	Retrospective comparative cohort	Unresectable liver tumors with/without prior hepatectomy	Resin/NR	2/427	General cohort	Yes
Geisel 2014 [22]	Retrospective cohort	Hepatic malignancies; 9 with biliodigestive anastomosis	Not reported	1/143	General cohort	Yes
Sag 2014 [23]	Retrospective consecutive gallbladder-effects cohort	Primary (34) and metastatic (99) hepatic tumors; gallbladder in situ	Resin 95; glass 38	1/133	General cohort	Yes
Lee 2015 [24]	Retrospective cohort	Advanced inoperable HCC	Not reported	1/30	General cohort	Yes
Powerski 2015 [6]	Retrospective comparative technical cohort	Liver malignancies with CA management data	Not reported	3/105	Anatomy/management enriched	Yes
Damm 2016 [25]	Retrospective cohort	Chemo-refractory liver-dominant metastatic colorectal cancer	Resin	1/106	General cohort	Yes
Kim 2016 [26]	Retrospective single-center cohort	Liver-dominant metastatic pancreatic adenocarcinoma	Not reported	1/16	General cohort	Yes
Mosconi 2016 [27]	Retrospective cohort with prospectively acquired follow-up data	Unresectable/recurrent intrahepatic cholangiocarcinoma	Not reported	1/23	General cohort	Yes
Parakh 2016 [3]	Retrospective cohort	Hepatic malignancies	Resin	4/74	General cohort	Yes
Pieper 2016 [28]	Retrospective single-center cohort	Advanced breast cancer liver metastases	56 resin and 13 glass treatment sessions	1/44	General cohort	Yes
Pieper 2016 [29]	Retrospective imaging/outcomes cohort	Breast cancer liver metastases	Resin	0/21	General cohort	Yes
Klompener 2017 [30]	Retrospective cohort	Intermediate/advanced HCC refractory to DEB-TACE	Not reported	1/30	General cohort	Yes

Study	Design	Population	Microspheres	Events/patients	Cohort type	Meta-analysis
Piasecki 2019 [31]	Quantitative anatomic/imaging cohort	Hepatic malignancies	Not reported	0/64	Anatomy/management enriched	Yes
Topcuoglu 2019 [32]	Retrospective technical cohort	Hepatic malignancies with CA near treatment territory	Glass	0/29	Anatomy/management enriched	Yes
Ebadi 2020 [33]	Retrospective consecutive cohort	HCC	Not reported	1/101	General cohort	Yes
Padia 2020 [7]	Retrospective multi-institutional feasibility cohort	HCC supplied by the cystic artery	Not reported	0/17	Anatomy/management enriched	Yes
Teyateeti 2020 [34]	Retrospective HCC cohort	Unresectable HCC	Glass	1/155	General cohort	Yes
Yammine 2020 [35]	Retrospective single-center cohort	HCC 8, cholangiocarcinoma 4, other metastases 11	Not reported	1/23	General cohort	Yes
Loffroy 2021 [36]	Prospective multicenter observational registry (CIRT-FR)	HCC 114; mCRC 38; ICC 33; other 15	Resin	0/200	General cohort	Yes
Mulcahy 2021 [37]	Randomized open-label international phase III trial (TARE arm safety cohort)	Second-line colorectal liver metastases	Resin	2/187	General cohort	Yes
Paprottka 2021 [38]	Retrospective cohort	Unresectable intrahepatic cholangiocarcinoma	Resin	0/73	General cohort	Yes
Paz-Fumagalli 2021 [39]	Retrospective ablative cohort	Unresectable intrahepatic cholangiocarcinoma	Glass	1/28	General cohort	Yes
Pellegrinelli 2021 [40]	Retrospective single-center cohort	HCC 44; mCRC 20; cholangiocarcinoma 6	Resin or glass	1/70	General cohort	Yes
Chaikajornwat 2022 [41]	Retrospective single-center cohort	Unresectable HCC	Not reported	0/52	General cohort	Yes
Minor 2022 [42]	Prospective pilot trial	Metastatic uveal melanoma	Resin	1/26	General cohort	Yes
Mosconi 2022 [43]	Retrospective longitudinal cohort	HCC	Not reported	3/253	General cohort	Yes
Yim 2022 [44]	Retrospective real-world cohort	Unresectable HCC	Not reported	1/149	General cohort	Yes
Carrión 2023 [45]	Retrospective consecutive cohort	HCC	Not reported	1/63	General cohort	Yes
Choi 2023 [8]	Retrospective direct-CA treatment cohort	HCC with parasitized cystic-artery supply	Not reported	0/24	Anatomy/management enriched	Yes
Damm 2023 [4]	Prospective consecutive management-algorithm cohort	Advanced liver tumors receiving right-lobe Y90 with gallbladder at risk	Not reported	4/130	Anatomy/management enriched	Yes
Maleux 2023 [46]	Prospective multicenter observational CIRT registry	HCC 422; ICC 120; mCRC 237; other metastases 248	Resin	4/1027	General cohort	Yes
Alexander 2024 [47]	Retrospective cohort	Primary lung cancer metastases to liver	Resin 34 patients; glass 23	2/57	General cohort	Yes
Karaoğullarından 2024 [48]	Retrospective single-center age-comparison cohort	HCC; 90 younger and 56 elderly patients	Not reported	6/146	General cohort	Yes
Kim 2026 [49]	Retrospective flow-redistribution cohort	HCC requiring inferior phrenic artery flow redistribution	Not reported	2/37	Technique enriched	Yes
di Gaeta 2026 [50]	Retrospective two-center dosimetry cohort	HCC	Resin	1/64	General cohort	Yes

Study Characteristics

The 44 reports were published from 2004 through 2026. Thirty-four were general clinical cohorts, seven were anatomy- or management-enriched cohorts, two were general mapping cohorts, and one was a flow-redistribution cohort. Study populations included hepatocellular carcinoma, intrahepatic cholangiocarcinoma, and multiple metastatic liver malignancies. Twenty-five reports explicitly captured all-grade symptomatic events; 19 used narrower or less complete adverse-event ascertainment. Microsphere type was not reported or not separable in 23 reports, limiting product-specific comparisons.

Incidence of Symptomatic Cholecystitis

The primary model included 43 independent cohorts, 5,380 patients, and 67 symptomatic cholecystitis events. The pooled incidence was 1.32% (95% profile-likelihood CI, 0.88%–1.89%). The crude aggregate proportion was 1.25% (67/5,380; exact 95% CI, 0.97%–1.58%), but this value does not account for between-study heterogeneity.

Heterogeneity and Sensitivity Analyses

Between-study heterogeneity was moderate (tau, 0.802; tau-squared, 0.643 on the logit scale; I-squared, 50.4%). The approximate 95% prediction interval was 0.28%–6.05%, indicating that incidence in a future clinically comparable cohort may differ substantially according to sampling frame, patient selection, anatomy, treatment technique, outcome definition, and follow-up.

Sensitivity analyses were consistent with the primary result. General and mapping cohorts yielded a pooled incidence of 1.21%, whereas anatomy- and technique-enriched cohorts yielded 2.65%. This contrast is descriptive because enriched cohorts were selected for cystic-artery proximity, gallbladder risk, or unusual treatment geometry. Leave-one-out estimates ranged from 1.24% to 1.46%, so no individual cohort determined the pooled estimate.

Table 2

Primary and sensitivity analyses. The primary CI was obtained by profile likelihood; sensitivity-analysis CIs were Wald intervals. Prediction intervals are approximate inverse-logit transformations of the fitted mean plus or minus 1.96 tau.

Analysis	Cohorts	Events/patients	Pooled incidence (95% CI)	I ²	95% prediction interval
independent eligible cohorts	43	67/5380	1.32% (0.88%–1.89%)	50.4%	0.28%–6.05%
General/mapping cohorts only	35	55/4928	1.21% (0.80%–1.81%)	50.3%	0.25%–5.59%
Anatomy/technique-enriched cohorts	8	12/452	2.65% (1.51%–4.62%)	0.0%	2.65%–2.65%
Explicit all-grade symptomatic ascertainment	25	38/3314	1.32% (0.76%–2.28%)	59.3%	0.20%–8.26%
Exclude ischemic/uncertain-causality cohorts	40	62/5283	1.21% (0.82%–1.79%)	50.1%	0.26%–5.53%
Modern era (2015 onward)	32	45/3424	1.42% (0.95%–2.10%)	35.1%	0.43%–4.54%

Figure 2 Study-specific symptomatic cholecystitis incidence with exact binomial 95% confidence intervals. Marker area is proportional to the square root of cohort size. The diamond shows the one-stage random-intercept binomial-normal generalized linear mixed-model estimate of 1.32% (95% CI, 0.88%–1.89%).

Procedural Factors

Catheter position relative to the cystic-artery origin provided the clearest quantitative procedural signal, although the reported endpoint was technetium-99m macroaggregated albumin leakage rather than clinical cholecystitis. Piasecki et al. [31] reported leakage in 12 of 34 proximal positions and 4 of 31 distal positions (P=.039; reported risk ratio approximately 2.5, 95% CI, 1.2–5.4). When tumor coverage can be preserved, distal positioning is therefore the most directly supported technical maneuver.

Comparative evidence did not support routine permanent cystic-artery coil embolization. Powerski et al. [6] reported similar event rates after coiling and no coiling (2/68 vs 1/37). McWilliams et al. [2] observed events in 2 of 11 coil-treated patients and 1 of 35 patients treated with temporary Gelfoam; the small, nonrandomized series raises concern for ischemic injury and collateralization after permanent occlusion. An algorithm-guided strategy did not significantly reduce events compared with standard care (2.9% vs 4.7%; P=.53) [4].

Gallbladder uptake and post-treatment imaging changes had low specificity for clinical disease. Sag et al. [23] found gallbladder imaging abnormalities in 84 of 85 evaluated cases but only one clinical event among 133 patients. Topcuoglu et al. [32] reported uptake in 11 of 34 procedures and no grade 2 or higher clinical events among 29 patients. Intentional treatment through cystic-artery tumor supply caused wall thickening or right-upper-quadrant pain in selected patients but no invasive cholecystitis in the Padia et al. [7] and Choi et al. [8] series. These reports show feasibility in selected expert-center cases and should not be extrapolated to inadvertent reflux.

Timing and Clinical Course

Clinical presentation varied with the suspected mechanism. In the Damm et al. [4] cohort, two presumed embolic events occurred within 48 hours and two presumed radiogenic events occurred later. Parakh et al. [3] described four cases presenting more than four weeks after treatment, all eventually

requiring cholecystectomy. Other cohorts reported onset within days or within the first month. The available evidence therefore supports early assessment for ischemic or embolic injury and continued attention to delayed radiogenic presentations.

Management ranged from observation, analgesia, and antibiotics to prolonged admission, percutaneous intervention, or cholecystectomy. Reporting was too inconsistent to estimate treatment-specific frequencies. No included report attributed a death directly to cholecystitis, although absence of reported event-specific mortality should not be interpreted as proof of no risk.

Procedural Evidence

Table 3

Evidence on procedural factors and preventive strategies. These nonrandomized comparisons were synthesized narratively and were not pooled. CA, cystic artery; MAA, macroaggregated albumin; RUQ, right upper quadrant.

Study	Factor	Comparison	Result	Interpretation
Damm 2023	Algorithm-guided prophylaxis	2.9% algorithm vs 4.7% standard care	P=.53; no demonstrated reduction	Selective algorithm is feasible; benefit remains uncertain
Powerski 2015	Permanent CA coil embolization	2/68 coiled vs 1/37 uncoiled	2.9% vs 2.7%; no significant difference	Routine permanent coil embolization is unsupported
McWilliams 2011	Coil vs temporary Gelfoam CA embolization	2/11 coil vs 1/35 Gelfoam	One coil patient required cholecystectomy	Small nonrandomized cohort; ischemic injury/collateralization are concerns
Piasecki 2019	Catheter position relative to CA	MAA leak 12/34 proximal vs 4/31 distal	P=.039; reported RR ≈ 2.5 (95% CI 1.2–5.4)	Distal catheter positioning is the clearest quantitative procedural signal
Sag 2014	Imaging abnormality / microsphere type	84/85 imaging abnormalities vs 1/133 clinical event	Clinical event followed glass infusion proximal to CA origin	Imaging findings are highly nonspecific; product inference is not possible
Topcuoglu 2019	Gallbladder uptake/dose without CA occlusion	11/34 procedures with uptake; 0/29 grade ≥ 2 clinical events	Mean gallbladder dose 96.4 ± 53.4 Gy	Uptake/dose alone did not predict symptoms
Padia 2020	Direct/ablative infusion via CA	0/17 invasive cholecystitis; RUQ pain 4/17	Median target dose 340 Gy	Feasible in selected expert-center cases; not evidence about inadvertent reflux
Choi 2023	Direct CA infusion branch	0/24 invasive cholecystitis; wall thickening 12/24	Main/deep/small feeder infusion	Selected direct-CA treatment can be clinically tolerated despite imaging changes

Small-Study Effects

The funnel display showed asymmetry, but interpretation is limited. For rare single proportions, the estimated effect and its standard error are mathematically dependent, and zero-event studies form a characteristic boundary. The plot therefore cannot distinguish publication bias from event rarity, cohort size, case-mix, and clinical heterogeneity. Egger and Begg tests were not performed.

Figure 3 Exploratory display of continuity-corrected logit incidence against precision. This figure explores small-study patterns; it is not a measure of heterogeneity and was not used as a formal publication-bias test. Heterogeneity is reported with tau-squared, I-squared, and the prediction interval.

Risk of Bias

The initial appraisal classified three reports as low overall risk of bias, 40 as having some concerns, and one as high risk. Common limitations were unclear selection, incomplete outcome definitions, uncertain capture of all symptomatic grades, and limited applicability of enriched cohorts.

Figure 4 JBI-informed study-level risk-of-bias and applicability judgments for the 44 included reports. Green indicates low risk, amber indicates some concerns, and red indicates high risk.

Discussion

Principal Findings

This systematic review found that clinically symptomatic cholecystitis after Y-90 TARE is uncommon. Across 43 independent cohorts, the pooled incidence was 1.32%, and the crude aggregate risk was 1.25%. The estimate was stable in leave-one-out analyses. The prediction interval was much wider than the pooled confidence interval, which indicates that a future cohort may observe a materially different incidence when patient selection, vascular anatomy, catheter position, treatment territory, and adverse-event surveillance differ.

The distinction between general cohorts and anatomy- or technique-enriched cohorts is clinically important. The pooled rate in enriched cohorts was higher, but this should not be interpreted as a causal effect of the evaluated technique. These cohorts preferentially included patients with cystic-artery

proximity, gallbladder uptake, direct cystic-artery tumor supply, or other challenging anatomy. Their higher baseline risk is part of the indication for the intervention.

Mechanism and Procedural Interpretation

The evidence supports both radiogenic and ischemic mechanisms. Delayed cases, including those described pathologically by Parakh et al. [3], are compatible with progressive radiation injury. Very early events after cystic-artery manipulation or right-lobar treatment are more compatible with embolic or ischemic injury. In practice, the mechanisms can overlap, and imaging alone may not establish the cause.

Distal catheter positioning has the strongest direct procedural support, but even that evidence rests on a mapping surrogate rather than symptomatic events. The finding is anatomically plausible and aligns with reports linking proximal infusion to gallbladder exposure [23, 31]. Operators must still balance distal positioning against complete tumor coverage and avoidance of reflux into other branches.

Routine permanent cystic-artery coiling is not justified by the available comparative data. Coiling did not reduce events in Powerski et al. [6], and the McWilliams et al. [2] series suggests that permanent occlusion can itself contribute to ischemic injury or collateralization. Selective temporary embolization or an anatomy-based algorithm may be reasonable in specific cases, but evidence of clinical benefit remains uncertain. Direct cystic-artery treatment can be feasible in expert centers when that artery supplies tumor, yet those results do not establish safety for inadvertent nontarget delivery.

Clinical Implications

Pre-treatment angiography and technetium-99m macroaggregated albumin mapping should be interpreted together with cystic-artery anatomy and the planned treatment territory. When feasible without compromising tumor coverage, a treatment position distal to the cystic-artery origin may reduce gallbladder exposure. Gallbladder uptake or wall change should prompt procedural review and clinical correlation, but imaging abnormalities alone should not be labeled symptomatic cholecystitis.

After treatment, clinicians should consider cholecystitis in patients with persistent or focal right-upper-quadrant pain, fever, leukocytosis, or compatible imaging. Early symptoms may reflect embolic or ischemic injury, whereas radiogenic disease may present weeks later. Initial management can be conservative in stable patients, but severe or persistent cases may require drainage or surgery. The review does not support a single management algorithm because treatment reporting was sparse and noncomparative.

Limitations

Most evidence was retrospective, and adverse-event reporting was not designed specifically for cholecystitis. Clinical definitions, severity thresholds, follow-up, and attribution of radiation versus ischemia varied. Nineteen reports did not clearly capture all symptomatic grades. Microsphere type was frequently unreported, and adjusted comparisons of resin versus glass or segmental versus lobar treatment were unavailable.

The prediction interval uses the fitted mean and estimated between-study standard deviation but does not fully propagate parameter uncertainty. I-squared is transformation-dependent for rare proportions and should be interpreted with tau-squared, the prediction interval, and clinical differences between cohorts. The funnel plot is descriptive and cannot establish publication bias.

Take-home message

Symptomatic cholecystitis after Y-90 TARE is uncommon, and the available evidence supports careful mapping and distal catheter positioning when feasible rather than routine permanent cystic-artery coiling.

Conclusion

Symptomatic cholecystitis after Y-90 TARE occurs in approximately 1.3% of treated patients on average, although incidence varies across settings. Careful vascular mapping and distal catheter placement when oncologically and technically feasible are the best-supported preventive measures. Routine permanent cystic-artery coiling is not supported by comparative evidence, and gallbladder imaging abnormalities should not substitute for clinical diagnosis. Independent verification of study selection, extraction, and risk-of-bias judgments is required before journal submission.

Declarations

Author Contribution

Conceptualization: A.K. Methodology: A.K. and R.V. Investigation: A.K. and P.Y. Data curation: A.K., R.V. and P.Y. Formal analysis: A.K., R.V. and R.B. Visualization: A.K. Writing – original draft: A.K., R.V., P.Y. and R.B. Writing – review and editing: M.B., L.V., G.B., D.F. and A.B. Supervision: M.B., L.V., G.B., D.F. and A.B.

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Figures

Fig. 1 Study Selection Flow Chart

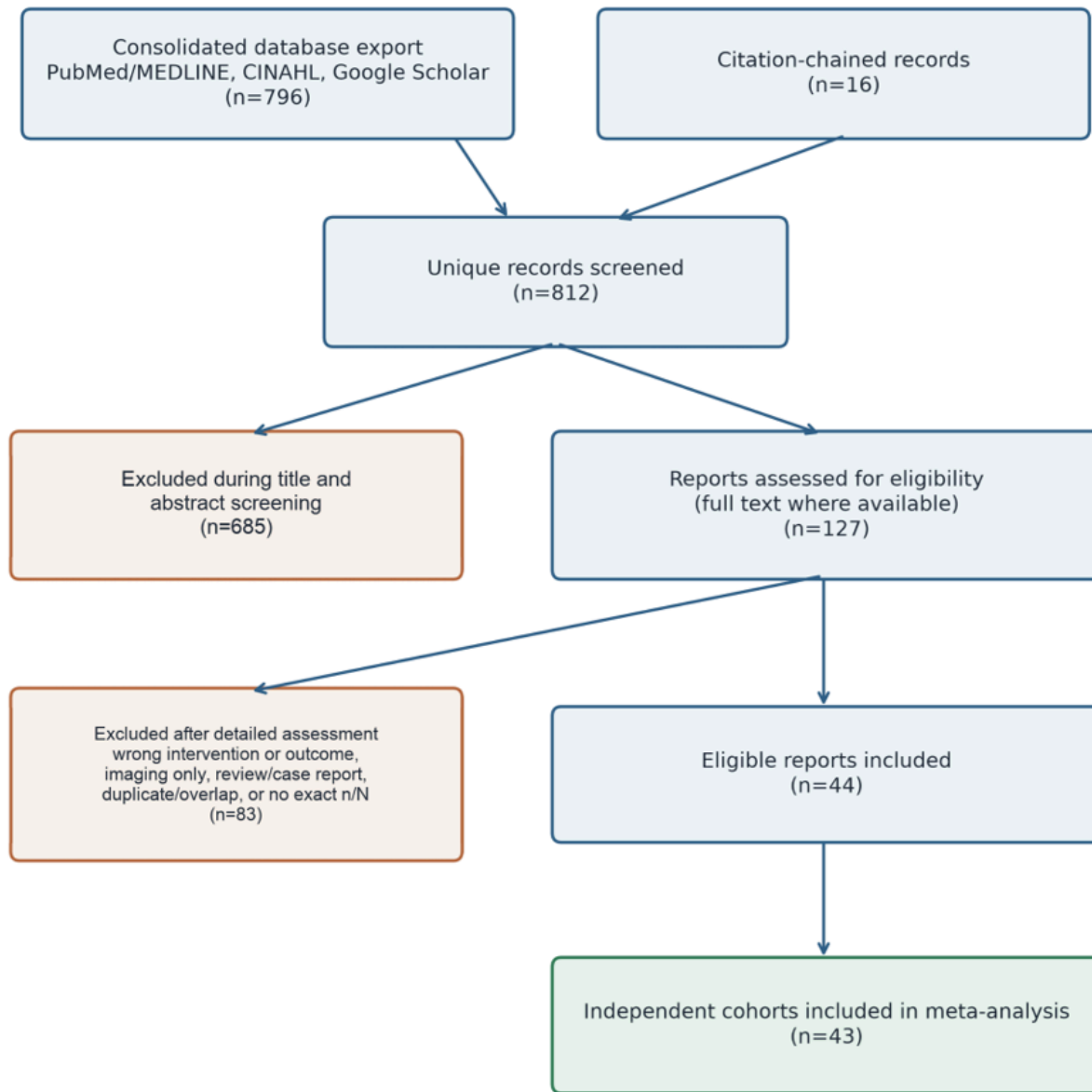


Figure 1

Study identification, screening, eligibility, and quantitative inclusion. The consolidated export was representing PubMed/MEDLINE, CINAHL, and Google Scholar. One likely overlapping report was excluded from the independent-cohort model.

Fig. 2 Forest Plot of Symptomatic Cholecystitis Incidence

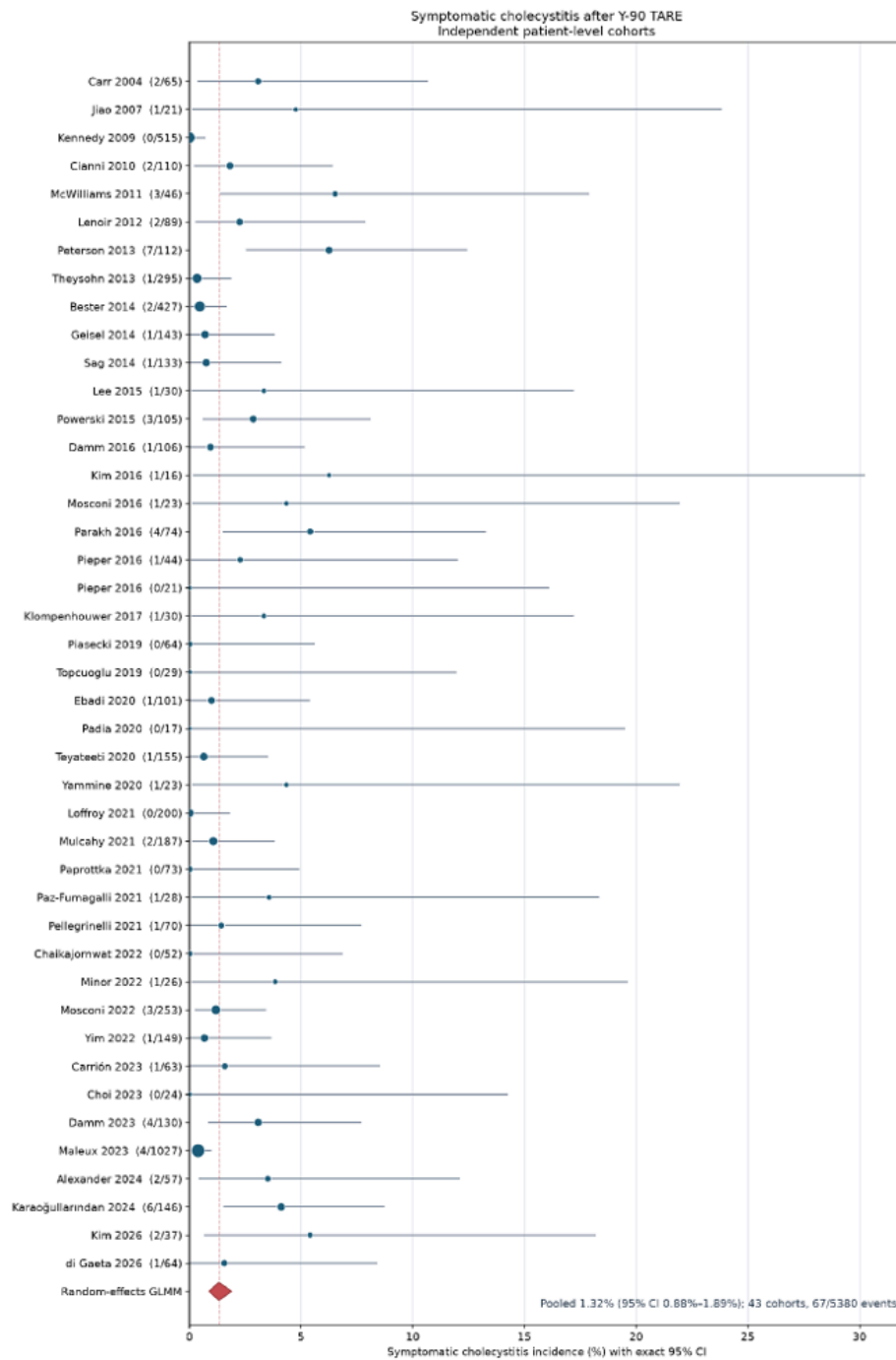


Figure 2

Study-specific symptomatic cholecystitis incidence with exact binomial 95% confidence intervals. Marker area is proportional to the square root of cohort size. The diamond shows the one-stage random-intercept binomial-normal generalized linear mixed-model estimate of 1.32% (95% CI, 0.88%–1.89%).

Fig. 3 Exploratory Funnel Plot

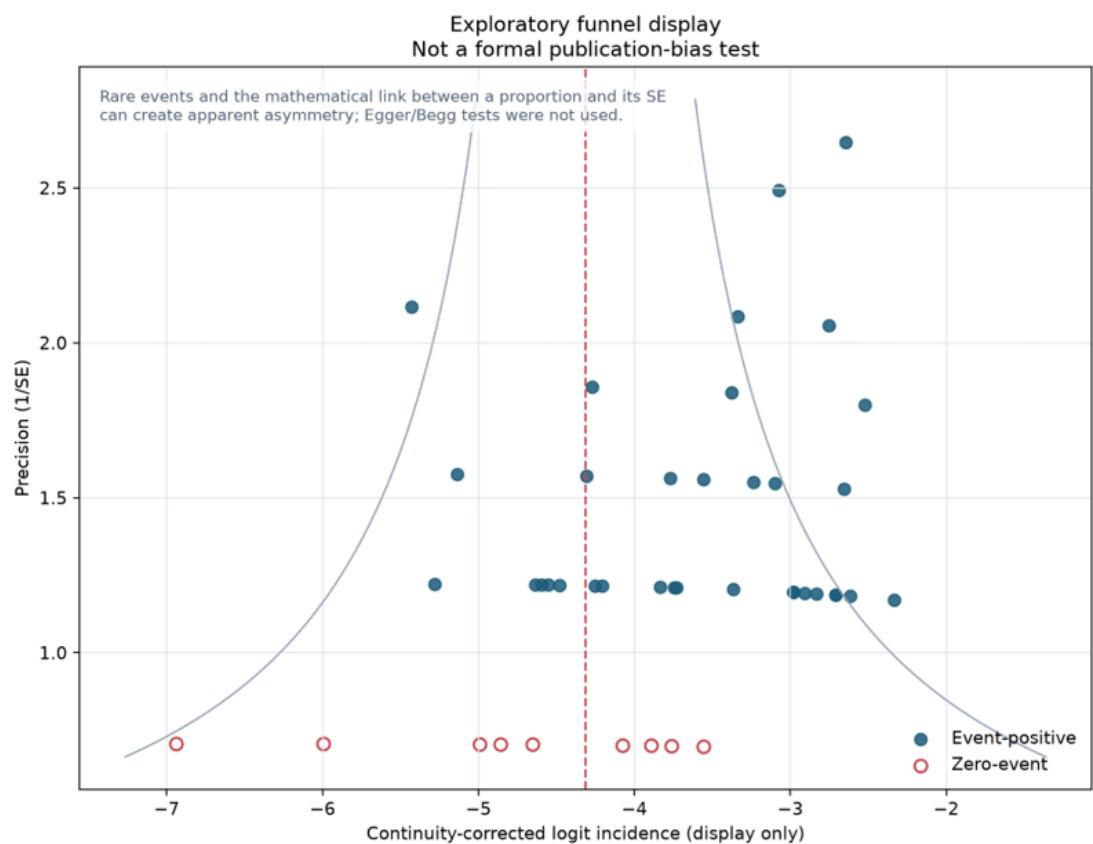


Figure 3

Exploratory display of continuity-corrected logit incidence against precision. This figure explores small-study patterns; it is not a measure of heterogeneity and was not used as a formal publication-bias test. Heterogeneity is reported with tau-squared, I-squared, and the prediction interval.

Fig. 4 Risk-of-Bias Stoplight Chart



Figure 4

JBI-informed study-level risk-of-bias and applicability judgments for the 44 included reports. Green indicates low risk, amber indicates some concerns, and red indicates high risk.

Supplementary Files

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